

## REMARKS

Claims 1-77 are pending in this application. Claims 45-48 have been withdrawn from consideration. Claims 1-44, 49-77 are rejected.

Claims 49-50, 52, 63-64, 70, 77 were rejected under 35 U.S.C. § 102(b). Claims 1-44, 51, 53-62, 65-69, 71-76 were rejected under 35 U.S.C. § 103(a).

### **Rejections under 35 U.S.C. §102(b)**

The Office rejected claims 49-50, 52, 63-64, 70 and 77 under 35 U.S.C. § 102(b) as being anticipated by Emmert-Buck, M. et al., "Laser Capture Microdissection", Science, Vol. 274, 8 Nov. 1996, pp. 998-1001 (hereinafter "Emmert-Buck"). Applicants traverse this rejection.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. MPEP § 2131. The preamble of independent claim 49 states that an "integral portion of a biological reaction vessel" is claimed. The preamble of independent claim 63 states that "a microcentrifuge tube cap, comprising an integral portion of a biological reaction vessel" is claimed. Independent claim 64 includes a LCM "cap". The preamble of claim 77 states that a "set of microcentrifuge tube caps" is claimed. As stated in the specification on page 4, lines 17-18, "there is a particular need for an LCM consumable that integrates an LCM film into the interior of an analysis container." Furthermore, at page 9, line 7, the specification states that the "sample carrier 300 can be a polymeric cap" and at page 18, lines 5-6, the specification states that the "cap 1120 is an integral portion of the biological reaction vessel 1100." At page 11, lines 5, the specification states that in "a preferred embodiment, the cap is sized to fit in a standard microcentrifuge tube. In one variation, the carrier is shaped like a cap for integration with a vessel to transfer the captured specimen for post LCM processing. Emmert-Buck does not disclose, teach or suggest an "integral portion of a biological reaction vessel", "a microcentrifuge tube cap", "a cap" and a "set

of microcentrifuge tube caps". In particular, a LCM carrier that is configured to mate with a biological reaction vessel or a microcentrifuge tube is not disclosed in Emmert-Buck. Therefore, Emmert-Buck does not anticipate claims 49, 50, 52, 63-64, 70, and 77 and the rejection should be withdrawn.

The Office directs attention to FIG. 1A of Emmert-Buck stating that Emmert-Buck discloses a LCM system comprising a transfer film carrier or cap. Applicants disagree. Although FIG. 1A of Emmert-Buck shows a transfer film, there is no disclosure of a carrier and much less of a carrier configured as a cap. The Office Action (Paper No. 20) includes an attached copy of Emmert-Buck in which the Examiner has drawn a lead line to FIG. 1A with the words "transfer film carrier" written next to it. This addition to the reference has no basis in the reference itself and applicants traverse an assertion by implication that a carrier or cap is disclosed. What is not present in the reference cannot be conveniently added. Nowhere in the reference is a carrier or cap disclosed.

#### **Rejections under 35 U.S.C. §103(a)**

The Office rejected claims 1-44, 51, 53-62, 65-69, 71-76 under 35 U.S.C. §103(a) as being unpatentable over Emmert-Buck in view of U.S. Patent No. 5,633,535 to Chao et al. (hereinafter "Chao"), or U.S. Patent No. 5,621,619 to Seffernick et al. (hereinafter "Seffernick"), or U.S. Patent No. 3,995,941 to Nagahara et al. (hereinafter "Nagahara").

In particular, with respect to claims 1, 15-16, 30-31, 44, the Office states that Emmert-Buck discloses the claimed invention except for the spacer or standoff to control the space." Paper No. 20, pg. 2. Applicants traverse this rejection. In order to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second,

there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations. MPEP §2143. To establish a prima facie case of obviousness, there must be some suggestion or motivation to modify or combine the reference teachings.

MPEP §2143. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in the applicant's discourse. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed.Cir. 1991).

As stated in the specification, "[t]here are a variety of techniques for building a noncontact LCM transfer film and/or carrier. The purpose of the noncontact LCM approach is to provide a method for the elimination of problems associated with nonspecific binding of tissue to an LCM film. In more detail, if a sample slide has areas with loosely attached cells, these portions of sample can be lifted mistakenly from the slide due to nonspecific attachment to the LCM film. That is, these areas stick to the film even though they were not illuminated by the laser. If these portions are transferred to the reagent vessel they will be digested by the reagents and appear as contaminants in the sample. It is important to prevent the loosely bound tissue areas from contacting the film. One method for preventing the contact of the film to areas of tissue that might nonspecifically transfer is to offset (distance) the film a few microns from the tissue sample." Specification, pg. 13, lines 11-21. Emmert-Buck, Chao, Seffernick, and Nagahara do not disclose, teach or suggest nonspecific transfer and ways of avoiding nonspecific transfer through noncontact LCM. In fact, Emmert-Buck teaches away from non-contact LCM by disclosing contact LCM as shown in FIG. 1A. There is no suggestion or motivation in Emmert-Buck for non-contact LCM and much less for forming protruding features to stand the LCM film from the sample as one form of non-contact LCM. Similarly, there is no suggestion or motivation in either Chao, Seffernick or Nagahara to employ noncontact LCM via protruding features.

Chao does not mention laser capture microdissection. Chao spaces an integrated circuit from a substrate. The two surfaces in Chao are attached with solder. Chao, col. 2, lines 52-55. Permanently soldering the two surfaces together as taught in Chao would render laser capture useless. Likewise, having separable surfaces as in LCM would render Chao useless. In fact, the solder bumps between the two surfaces are heated such that they melt to make permanent electrical connection with the contacts. It is this melting of the solder bumps that result in the two surfaces from being misaligned. "When heated, the bumps will reflow and the chip floats on the solder." Chao, col. 1, lines 31-32. Chao uses pedestals to keep the substrate at an equal spacing from the integrated circuit. In contrast, the present invention uses protruding features to avoid non-specific transfer. Chao is at cross-purposes with laser capture and the art is non-analogous. The references must be combinable. The claimed combination cannot change the principle of operation of the primary reference or render the reference inoperable for its intended purpose. MPEP §2143.01. Chao and Emmert-Buck render each other useless for their intended purposes. For these reasons, applicants believe these claims to be nonobvious.

Also, Nagahara does not mention laser capture microdissection. Nagahara pertains to liquid crystal cells and does not disclose teach or suggest protruding features for avoiding nonspecific transfer. In Nagahara, the two surfaces are spaced to form a cell in which a liquid crystal is retained. The two surfaces in Nagahara are permanently attached and are not separable. The two surfaces in Nagahara are sealed together. "[A] completely hermetic seal is ensured." Nagahara, col. 5, lines 50-51. "Thereafter, the resulting assembly is baked one-piece." Nagahara, col. 5, lines 14-15. The "planar element and the assembly is baked at a temperature of 400 °C to 550 °C for about half an hour to about 2 hours." Nagahara, col. 3, lines 23-25. A proposed modification cannot change the principle of operation of a reference. MPEP §2143.01. If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the

reference are not sufficient to render the claims prima facie obvious. The teachings of Nagahara would change the principle of LCM operation. In LCM, the tissue attached to the transfer film is lifted when the transfer film is removed. Similarly, the teachings of Emmert-Buck would change the principle of operation of Nagahara such that a removable surface in Nagahara would render Nagahara useless for its intended purpose of retaining a liquid crystal in between the surfaces. Nagahara, col. 5, lines 1-8. In LCM, the space between the two surfaces is not filled with liquid crystal, nor are the two surfaces sealed into one unit, nor is LCM performed with the two surfaces baking at temperatures that would destroy the tissue. There is no appreciation of LCM methods in Nagahara. In fact, Nagahara teaches away from LCM by sealing the two surfaces together without regard to tissue insertion, removal and cell capture. Doing so would render LCM useless. Nagahara uses pedestals to create an even cell for liquid crystal. The present invention uses protruding features to avoid non-specific transfer. Nagahara is at cross-purposes with laser capture and the art is non-analogous. The references must be combinable. Nagahara and Emmert-Buck render each other useless for their intended purposes. For these reasons, applicants believe these claims to be nonobvious.

Seffernick pertains to surface mount resistors. Seffernick does not discuss laser capture microdissection. There must be a suggestion or motivation in the reference themselves in order to establish prima facie case for obviousness. There is no hint of LCM in Seffernick. There is no hint of forming protruding features in Emmert-Buck. Hindsight cannot be used and the references must be combinable without rendering each other useless for their intended purposes. In Seffernick, solder bumps are spaced by stand-offs to prevent solder bridging between terminations. Seffernick, col. 3, lines 56-58. Using solder to affix the transfer film to the tissue sample carrier would render LCM useless. A removable surface in Seffernick would render Seffernick useless for establishing an electrical contact. Similarly to Chao, Seffernick uses stand-offs to space an integrated circuit from a substrate such that when solder melts the surfaces

are evenly spaced apart. The present invention uses protruding features to avoid non-specific transfer. Seffernick is at cross-purposes with laser capture and the art is non-analogous. The references must be combinable. Seffernick and Emmert-Buck change the principle of operation of each rendering them useless for their intended purposes. For these reasons, Seffernick and Emmert-Buck do not render the present invention obvious.

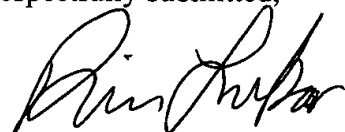
Furthermore, in order to establish a prima facie case of obviousness the prior art reference must teach or suggest all of the claimed limitations. Emmert-Buck, Chao, Nagahara and Seffernick do not disclose, teach or suggest the claim limitations of a microcentrifuge tube cap, an integral portion of a biological reaction vessel, and a cap. For these, reasons, the prior art does not render the present invention obvious and applicants believe that the application is in a condition for allowance and earnestly request action towards that end.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 4857772000400.

Respectfully submitted,

Dated: April 23, 2001

By:



Rimas T. Lukas  
Registration No. 46,451

Morrison & Foerster LLP  
755 Page Mill Road  
Palo Alto, California 94304-1018  
Telephone: (650) 813-5905  
Facsimile: (650) 494-0792